Apr 29 1980

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

ORDER AND NOTICE

Dear Registrant:

EPA recently completed a review of the available scientific information on the potential health effects of 2,4-D.

On April 29, 1980, based on the findings of the review, the Agency announced that significant gaps exist in the data base for 2,4-D and that additional scientific information will be required from the registrants under Section 3(c)(2)(B) of Federal Insecticide Fungicide Rodenticide Act (FIFRA), 7 U.S.C. 136a(c)(2)(B). This provision allows the Administrator of EPA to request any additional data from pesticide registrants that is considered necessary to maintain the registration of existing products. Enclosed is a copy of the Fact Sheet on 2,4-D which outlines the results of the Agency's review of the scientific information and the decision to require new studies under Section 3(c)(2)(B). Since this Fact Sheet was prepared for the general public, it may contain information which you already know. However, we feel that the Fact Sheet will provide you with material which will clarify EPA's reasons for requesting additional data from you.

Our records indicate that you are the registrant of a pesticide product(s) containing one or more of the following active ingredients which we will refer to collectively as 2,4-D:

2,4-dichlorophenoxyacetic acid
lithium salt of 2,4-D
potassium salt of 2,4-D
sodium salt of 2,4-D
ammonium salt of 2,4-D
alkanol amine salt of 2,4-D

alkyl amine (C12) salt of 2,4-D
alkyl amine (C14) salt of 2,4-D
alkyl amine (fatty acids
of tall oils) salt of 2,4-D
diethanolamine salt of 2,4-D
diethylamine salt of 2,4-D
dimethylamine salt of 2,4-D
dimethyloleylamine of 2,4-D
ethanolamine salt of 2,4-D
heptylamine salt of 2,4-D
isopropanolamine salt of 2,4-D
isopropylamine salt of 2,4-D
morpholine salt of 2,4-D
oleyl propylenediamine salt of 2,4-D
octylamine salt of 2,4-D
triethanolamine salt of 2,4-D
triethylamine salt of 2,4-D
triisopropanolamine salt of 2,4-D
diethylethanolamine salt of 2,4-D
dimethyloleylo-linoleylamine salt
butoxyethoxypropyl ester of 2,4-D
butoxyethyl ester of 2,4-D
butoxypolyethoxypropyl ester of 2,4-D
butoxypropyl ester of 2,4-D
butyl ester of 2,4-D
isobutyl ester of 2,4-D
isooctyl (ethyl hexyl) ester of 2,4-D
isooctyl (ethyl methyl pentyl) ester of 2,4-D
isooctyl (octyl) ester of 2,4-D
isopropyl ester of 2,4-D
propylene glycol butyl ether ester (PGBE) of 2,4-D

A list of your products that contain any of these materials is shown as Appendix A. Also refer to Appendix H for state registrations under Section 24(c)(1) for special local need which are also covered by this letter.

I. REQUIREMENT FOR DATA SUBMISSION

As we have explained in the Fact Sheet, under the authority of Section 3(c)(2)(B) of FIFRA, EPA has determined that additional data, more fully described in Section II of this letter, are required to maintain your registration(s) in effect.

This letter notifies you that if you wish your registrations to be maintained in effect, you are required to take steps to produce and submit data to EPA in accordance with the schedule set forth in Section III of this letter.

Sections IV and V of this letter indicate two limited circumstances in which EPA will not act to suspend the registration of your products if you do not submit the required data. Section VI of this letter describes the procedures by which you may ask EPA to reconsider the requirements imposed by this letter.

In responding to the data requirements established by this letter, you must choose one of the following options. If you fail to exercise one of these options within the time period specified, EPA may take steps to suspend the registration of each product to which the required data are pertinent.

(A) You must notify EPA within 90 days of your receipt of this letter that you are willing to produce (if necessary) and submit the data yourself;

(B) You must notify EPA within 90 days of your receipt of this letter that you have entered into an agreement, with one or more of the other registrants who are subject to this notice's requirements, to jointly produce (if necessary) and submit the data, or to share in the cost of this work;

(C) You must provide to EPA, within 90 days of your receipt of this letter, the "Statement of Willingness to Enter Into an Agreement with Other Registrants for Development of Data", in accordance with Section V and Appendix C of this letter, which will allow EPA to exempt you from the consequences of not submitting some or all of these data under certain circumstances;

(D) You must provide to EPA, within 30 days of your receipt of this letter, the Certification described in Section IV of this letter, which will allow EPA to exempt you from the consequences of not submitting some or all of these data because each of your products is an end-use product and otherwise qualifies under that Section;

(E) You must file with EPA, within 30 days of your receipt of this letter, a request for a waiver of some or all of the data requirements imposed by this Order and Notice; or,

(F) You must file with EPA, within 90 days of your receipt of this letter, a request that the registration(s) for your products containing any or all forms of 2,4-D be voluntarily cancelled.

II. WHAT DATA ARE NEEDED

EPA has determined that significant gaps exist in the data base for pesticides containing 2,4-D compounds. In order to make further determinations concerning potential health effects of 2,4-D, the Agency has determined that data from the studies listed below are required to support the continued registration of all products containing the various forms of 2,4-D. The required studies must be conducted in accordance with the referenced sections of EPA's proposed pesticide registration guidelines,*/ or other approved test standards such as those which are adopted by the Organization for Economic Cooperation and Development (OECD) except as modified or supplemented below.**/

TOXICOLOGY DATA

The following section describes the tests to be conducted and the specific forms of 2,4-D to be tested. When performing studies to produce the required data, you should be very careful to follow every applicable test standard contained either in the section of the guidelines cited or other approved test standards, except as modified in the paragraphs below.

COMPOUNDS TO BE TESTED

Some of the data requirements relate to specific technical grade forms of 2,4-D, while other tests pertain to formulated products. Because the salt and ester forms of 2,4-D will degrade to the acid form and to the metabolite 2,4-dichlorophenol, registrants of products containing any salt or ester form will be responsible for all the required studies on technical grade 2,4-dichlorophenoxyacetic acid and on 2,4-dichlorophenol. (See Appendix G). The required studies on the other technical grade forms of 2,4-D are the responsiblity of those registrants whose products contain

*/ The Agency published proposed human hazard guidelines on August 22, 1978, 43 FR 37336. The required studies on 2,4-D (with the exception of subacute dermal neurotoxicity, standard metabolism in pregnant dogs, and dermal absorption) are described in this section. Copies of the proposed guidelines are available on request.

**/ Note: you may request EPA to review the use of a test method which may vary from the test standards listed above in order to produce the required data. The procedures for submitting such a request are described in Section VI of this letter.

those compounds as active ingredients. The required studies on each formulated product, regardless of the specific forms of 2,4-D it contains, are the responsibility of the registrant to whom that product is registered.

DATA REQUIREMENTS

1. Oncogenicity studies - standard oral exposure study in rats and mice (proposed Section 163.83-2, 43 FR 37379-82).

   Material to be tested:
   - technical grade (or purer) of 2,4-dichlorophenoxycetic acid

   Note: All registrants are responsible for this data*/

2. Reproduction study - (proposed Section 163.83-4, 43 FR 37384-88).

   Material to be tested:
   - technical grade (or purer) of 2,4-dichlorophenoxyacetic acid

   Note: All registrants are responsible for this data*/

3. Teratogenicity studies - (proposed Section 163.83-3, 43 FR 37382-84) modified as follows: test to be done in the rat.

   Materials to be tested:
   - technical grade (or purer) of 2,4-dichlorophenoxyacetic acid
   - technical grade (or purer) of butoxypropyl ester of 2,4-D
   - technical grade (or purer) of alkanolamine salt of 2,4-D
   - technical grade (or purer) of isopropyl ester of 2,4-D
   - 2,4-dichlorophenol (metabolite of 2,4-D)

   Note: All registrants are responsible for the data on 2,4-D acid and the metabolite, 2,4-dichlorophenol. Registrants with products containing the salt and ester forms listed above are also responsible for the data on those forms of 2,4-D.*/

4. Neurotoxicity studies

   a) subchronic oral neurotoxicity - (proposed Section 163.82-5, 43 FR 37374-75) modified as follows: test to be done in the dog, rat, and chicken. Materials to be tested:

      - technical grade (or purer) of 2,4-dichlorophenoxyacetic acid
      - technical grade (or purer) of dimethylamine salt of 2,4-D

*/ Registrants of end-use products formulated from a registered technical material should consult Section IV for exemption from this requirement.

Note: All registrants are responsible for the data on 2,4-D acid. Registrants with products containing the dimethylamine salt of 2,4-D are responsible for the data on this form.*/

b) subacute dermal neurotoxicity in the dog - This study will be required for the two compounds described in (a) unless otherwise indicated by the results of the subchronic neurotoxicity study and the results of dermal absorption study on that compound. EPA will review the results of these tests when submitted and inform the registrants whether to proceed with (b). At that time, registrants will be notified of the protocol to be used in developing this data.

5. Metabolism studies

a) standard metabolism study - (proposed Section 163.85-1, 43 FR 37394-96) modified as follows: test to be done in the dog and rat. Materials to be tested:

- technical grade (or purer) of 2,4-dichlorophenoxyacetic acid
- technical grade (or purer) of isooctyl (ethylhexyl) ester of 2,4-D
- technical grade (or purer) of PGBE ester of 2,4-D

Note: All registrants are responsible for this data on 2,4-D acid. Registrants with products containing one of the two ester forms listed above are also responsible for the data on those forms.*/

b) standard metabolism study in the pregnant dog - This study will be required for the three compounds described in (a) unless otherwise indicated by the results in (a). EPA will review the results of this test when submitted and inform the registrants whether to proceed with (b). At that time, registrants will be notified of the protocol to be used in developing this data.

6. Acute oral toxicity studies - (proposed Section 163.81-1, 43 FR 37355-56). Materials to be tested:

- each manufacturing-use product and each end-use product containing any of the 2,4-D compounds (Refer to Appendix A for the list of your products

*/ Registrants of end-use products formulated from a registered technical material should consult Section IV for exemption from this requirement.

for which this data must be submitted). A registrant may cite acceptable studies previously submitted to support the registration of his product(s). In lieu of providing his own studies, a registrant may cite acceptable studies already on file with the Agency or submit studies on a substantially similar product, and offer to compensate for such studies.

7. Acute dermal toxicity studies - (proposed Section 163.81-2, 43 FR 37356-57). Materials to be tested:

- each manufacturing-use product and each end-use product containing any of the 2,4-D compounds (Refer to Appendix A). A registrant may cite acceptable studies previously submitted to support the registration of his product(s). In lieu of providing his own studies, a registrant may cite acceptable studies already on file with the Agency or submit studies on a substantially similar product, and offer to compensate for such studies.

Note: The Agency generally requires a series of acute toxicity tests to support the registration of manufacturing use and formulated products. Acute oral toxicity and acute dermal toxicity studies are required for each manufacturing use product and each formulated product. Acute inhalation toxicity, primary eye irritation, primary dermal irritation, and dermal sensitization studies may be required to support the registration of each manufacturing use product and each formulated product, as specified in the proposed pesticide registration guidelines.

While the Agency is requiring only acute oral toxicity and acute dermal toxicity studies at this time, the other acute studies may be required at a later date as appropriate. The data which are being required at this time are essential to provide the Agency with a more accurate and detailed picture of any potentially significant acute oral and/or chronic health effects of 2,4-D. The Agency feels that acute oral and dermal toxicity studies will make a substantial contribution to our understanding of the acute hazard that may be associated with the chemical.

8. Dermal absorption studies -

At this time the Agency does not feel an acceptable protocol has been developed for testing pesticides. Therefore, although this testing remains a requirement as outlined in this letter, you will be notified at a later date of the protocol to be used in developing this data.

Materials to be tested:

- each end-use product formulated in liquid form or as an emusifiable concentrate that contains any of the 2,4-D compounds. (Refer to Appendix D for the list of your products for which this data must be submitted).

III. SCHEDULE FOR SUBMITTING DATA

The required data must be submitted to the Agency on the following schedule. If progress reports are required, the schedule will specify the date on which the first progress report is due, and the frequency of progress reports thereafter. If required, progress reports must be provided as specified below. Note: You may request that EPA extend any of the following deadlines. The procedures for submitting such a request are described in Section VI of this letter.

1. Oncogenicity studies

Final report due by 12/1/83
Progress report due on 6/15/82

2. Reproduction studies

Final report due by 3/1/82
Progress report due on 1/1/82 (for the two litters of the first generation)

3. Teratogenicity studies

Final report due by 6/10/81

4. Neurotoxicity studies

a) subchronic oral neurotoxicity
Final report due by 9/1/81

b) subacute dermal neurotoxicity - Registrants will be notified of the due date when they are notified whether to proceed with this testing.

5. Metabolism studies

a) standard metabolism
Final report due by 5/10/81

b) standard metabolism in pregnant dog - Registrants will be notified of the due date when they are notified whether to proceed with this testing.

6. Acute oral toxicity studies

Final report due by 5/1/81

7. Acute dermal toxicity studies

Final report due by 5/1/81

8. Dermal absorption studies

Registrants will be notified of the due date at the same time they are notified to proceed with this testing according to the specified protocol.

IV. REGISTRANT RESPONSIBILITY FOR SUBMISSION OF DATA AND EXEMPTION FROM SUSPENSION SANCTION FOR CERTAIN END-USE PRODUCT REGISTRATIONS

The data described in Section II of this letter relates, in certain cases, to the safety of specific 2,4-D active ingredients (technical grade). According to Section 3(c)(2)(D) of FIFRA, an applicant for registration of an end-use product containing one or more of these forms of 2,4-D is not required to submit or pay compensation for those data as a condition of obtaining registration if that form of 2,4-D is present in his product solely as the result of his incorporation into his product (as part of the formulation or packaging processes) of another registered product, containing that form of 2,4-D, which he purchases from another producer.

The object of this provision is to simplify data compensation by making compensation for data on active ingredient safety an element of the market cost of registered manufacturing-use products, so that formulators or other registrants who purchase such products need not separately offer to pay for data on the safety of the active ingredient.

EPA has concluded that these principles should also apply in the closely analogous situation presented by this Section 3(c)(2)(B) requirement. However, principles of fairness to those who incur expenses of data production and submission require that a registrant may be exempted from data submission requirements only if the specific form of 2,4-D in his product (listed on the active ingredient statement) is purchased from a firm which does have a duty to submit (or to offer to share in the cost of obtaining) the data required by this letter. (Refer to Appendix E for a list of firms with registered manufacturing-use products).

If a registrant who is subject to this Order and Notice fails to comply with the data submission requirement, the Administrator may suspend his registration. However, this authority is discretionary, and the Administrator will not exercise it to suspend a registration if:

(1) The registration is for an end-use product (as opposed to a manufacturing-use product) (Refer to Appendices F and G); AND, */ **/

(2) The specific form of 2,4-D in the end-use product is present solely as the result of the incorporation into that product (during formulation or packaging) of another product which contains that form of 2,4-D which is registered under FIFRA and which is purchased by the registrant; AND,

(3) The registrant completes and executes a "Certification of Entitlement to Exemption from Suspension Under FIFRA Section 3(c)(2)(B)", in the form of Appendix E to this letter, for each of his registered products containing some form of 2,4-D and submits it to EPA not later than September 30, 1980; AND,

(4) One or more registrants actually undertake to submit, and do submit, all the data required by this Order and Notice.

It should be emphasized that while the above procedures provide certain categories of exemptions, those data requirements that specifically relate to end-use (formulated) products are the responsibility of the registrant to whom that product is registered. (See Appendices A and D).

*/ Note: In the case of data requirements for technical grade forms of 2,4-D for which there are no registered manufacturing-use products, the registrants of the end-use products are responsible for the data.

**/ Note: Appendix F lists the company numbers for those registrants who have end-use products containing forms of 2,4-D for which there are no registered manufacturing-use products. Refer to Appendix G to obtain company names and addresses from the company numbers.

V. EXEMPTION FROM SUSPENSION SANCTION FOR REGISTRANTS WHO OFFER TO SHARE IN THE EXPENSE OF OBTAINING DATA

FIFRA Section 3(c)(2)(E) authorizes joint development of data by two or more registrants, and provides a mechanism by which parties can obtain an arbitrator's decision if they agree to jointly develop data but fail to agree on all the terms of the agreement. The statute does not compel any registrant to agree to develop data jointly.

In EPA's opinion, joint data development by all registrants who are subject to the requirements in this letter, or a cost-sharing agreement between all such registrants, is clearly in the public interest. Duplication of testing is not only wasteful in terms of money, but could tie up testing facilities unnecessarily.

As noted earlier, EPA has discretion not to suspend the registration of a product when a registrant fails to submit data required under FIFRA Section 3(c)(2)(B). EPA has concluded that it is appropriate to exercise its discretion not to suspend in ways which will discourage duplicative testing. Accordingly, if: (1) a registrant has informed us of its intent to develop and submit data required by this Notice and Order; and (2) a second registrant informs EPA that it has made a bona fide offer to the first registrant to share in the expenses of the testing (on terms to be agreed upon or determined by arbitration under FIFRA Section 3(c)(2)(B)(iii)); and (3) the first registrant has without good cause declined to agree to enter into a cost-sharing agreement, EPA will not suspend the second firm's registration. While the first firm is not required to agree to jointly develop data, EPA is not required to force the second firm to engage in economically inefficient duplicative testing in order to maintain its registration.

The format for informing EPA of the bonafide offer to the first registrant is shown as Appendix C.

VI. PROCEDURES FOR REQUESTING WAIVERS, CHANGES IN TESTING METHODOLOGY, AND EXTENSIONS OF TIME

EPA recognizes that you may disagree with our conclusions regarding the need for data, the appropriate ways to develop the required data, and how quickly the data must be submitted. We will give you the opportunity to state the basis for your disagreement and request that we change our requirements. We note that if you seek to challenge our requirements in court, a judge may

dismiss your lawsuit unless you have first presented your arguments to EPA according to the procedures described below.*/

If you think that EPA does not need the data required by this letter to determine whether your product causes unreasonable adverse effects on the environment, you may request a waiver. The waiver request must be submitted within 30 days of your receipt of this letter. The waiver request must be submitted in writing to the person specified at the end of this letter. The waiver request should state the reasons why you conclude that each particular kind of data is not needed. EPA will promptly review your request(s) and inform you whether the waiver has been granted.

If you want to use, or think that you should use, a test methodology which does not satisfy the test standards specified in Section II of this letter, you may ask EPA to review and approve that methodology. The request must be submitted in writing to the person specified at the end of this letter.

In most cases, EPA will not grant an extension of time to submit required data on the ground that you have requested Agency approval to change the required test methodology. Accordingly, you should submit the request as soon as possible.

If you want, or think that you will need, more time to produce the required data than is allowed by EPA's schedule, you must submit a request for an extension of time. The extension request must be submitted in writing to the person specified at the end of this letter. The extension request should state the reasons why you conclude that an extension is appropriate. No extensions will be granted based on the fact that the Agency is considering your request for an extension. Accordingly, you must continue to work diligently to meet the deadline for submitting the required data while EPA considers your request.

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*/ This letter constitutes "final Agency action" unless you submit a request for a waiver, a request for a modification in the required test methodology, or a request for extension of time. If any such request has been submitted, EPA's action with regard to the subject matter of the request does not become final until the Agency has acted on the request. The Agency thinks that a registrant must use the procedures described in this section of the letter in order to exhaust its administrative remedies.

VII. CONCLUSION

All responses to this notice should be submitted to:

Director, Special Pesticide Review Division (TS-791)
Office of Pesticide Programs
U.S. Environmental Protection Agency
401 M St., S.W. Washington, D.C. 20460

ATTN: 2,4-D Project Manager

If you have any questions regarding the requirements and procedures established by this letter, please contact:

Kevin Keaney, Chief, Chemical Review Branch #2, (703) 557-7716.

Sincerely yours,

Edwin L. Johnson
Deputy Assistant Administrator
for Pesticide Programs

Enclosures

4/22/80

2,4-D FACT SHEET

I. Background

2,4-D is one of the most widely used herbicides in the United States. There are approximately 1,500 products containing 2,4-D registered with EPA, and more than 70 million pounds of the active ingredient are distributed annually. The term "2,4-D" refers to the phenoxy herbicide 2,4-dichlorophenoxy acetic acid and its 35 derivative salt and ester forms. 2,4-D is used to control broadleaf weeds in a variety of places including home lawns, cereal and grain crops, commercial areas, commercial turf, rights-of-way, and forests.

Public concern about the potential adverse health effects of 2,4-D has intensified since the emergency suspension of 2,4,5-T and Silvex in March 1979. This concern stems primarily from 1) the chemical similarity of 2,4-D and 2,4,5-T as phenoxy herbicides, and 2) the question of 2,4-D dioxin-contamination, especially contamination with tetrachlorodioxin, a manufacturing contaminant in 2,4,5-T, which causes cancer and miscarriages. Due to the chemical similarity of 2,4-D and 2,4,5-T, the public has expressed concern about the potential for cancer and miscarriages from the use of 2,4-D. There is also concern because the controversial military defoliant Agent Orange, used in Viet Nam, was composed of 2,4,5-T and 2,4-D. Agent Orange was never registered by EPA for civilian use in the United States. Its use in Viet Nam by the U.S. military has resulted in claims of adverse health effects to American military personnel. The Veterans Administration is studying these claims.

Prompted by these concerns and EPA's need to resolve the questions surrounding the use of 2,4-D, the Agency initiated a review of the available information on the potential health effects of 2,4-D. This review was conducted in part to determine if the herbicide should be reviewed under the RPAR process (Rebuttable Presumption Against Registration) or if another regulatory action was appropriate.

II. Agency Review and Conclusions

Based on the results of this review, EPA has concluded that a) the presently available information on the potential adverse health effects of 2,4-D does not support a regulatory action to remove 2,4-D products from the market; b) information from scientifically valid studies does not indicate that the continued use of 2,4-D poses an imminent hazard or unreasonable adverse effect when used according to label precautions and direction for use; and c) the Agency should act quickly and vigorously to obtain better toxicological information on 2,4-D.

These conclusions are based on these following considerations:

1. There is no evidence available at this time that indicates 2,4-D contains any form of dioxin. This includes the tetrachloro-dioxin (TCDD), which is a manufacturing contaminant of 2,4,5-T and causes cancer and miscarriages.

TCDD is not theoretically expected to be found in 2,4-D. The manufacturing processes and starting chemicals from which 2,4-D and 2,4,5-T are made are not the same. Although other much less toxic dioxins are theoretically possible in 2,4-D, they have not been found despite thorough chemical analyses.

2. Because products containing 2,4-D have been registered for use since the 1940's, most of the scientific data submitted to support the product registrations now on the market were developed many years ago. While some of these studies are scientifically valid, many others do not meet today's standards for scientific testing. As a result, there are significant information gaps in several areas including cancer-potential, reproductive effects, neurotoxicity, and metabolism in animals.

3. The studies most pertinent to the question of tumor-causing potential (oncogenicity) of 2,4-D were considered inadequate and inconclusive. No valid conclusions could be drawn one way or another from the data.

4. Animal tests conducted on the potential reproductive effects of 2,4-D show that, unlike 2,4,5-T with its contaminant TCDD, severe life-threatening effects were generally absent from 2,4-D treatments at moderate or high doses. However, new tests will need to be conducted at lower doses to clearly establish no-effects levels. In comparison, TCDD, which is present in 2,4,5-T and not in 2,4-D, produces serious life-threatening effects on the fetus at minute doses including the lowest dose tested in many studies.

5. The scientific evidence available at this time does not indicate the potential human exposure is sufficient to result in human health effects.

6. The most vigorous authority available to EPA under the pesticide law to fill information needs is a new section of FIFRA (Federal Insecticide Fungicide Rodenticide Act) passed in 1978. This provision, known as 3(c)(2)(B), allows EPA to request any additional data from pesticide registrants that is considered necessary to maintain the registration of existing products. The Agency can immediately require the

manufacturers to develop the data where gaps exist. The registrants have 90 days to show that they are complying. Their product registrations may be summarily suspended if they fail to meet the Agency's conditions. No other action could obtain this information any faster. EPA is putting the data requirements into final form and they will be issued to the registrants after review by our Scientific Advisory Panel. These scientific experts will review and comment on the data requirements to assure that they will provide the information EPA needs to more definitively answer the questions on potential health effects of 2,4-D.

7. Based on a review of the toxicology data (see section IV below), and a review of the risks of other pesticide chemicals now undergoing regulatory action, the Agency believes that the risks of several other pesticides are higher and better documented than those associated with 2,4-D. To put the review of these other higher priority chemicals aside in order to devote EPA resources to taking action against 2,4-D would not, in the Agency's opinion, best serve the public interest.

III. Additional Actions

In addition to requiring several important studies of the manufacturers on 2,4-D, EPA will also:

1. Conduct several tests on reproductive effects (through our Office of Research and Development) of several derivatives of 2,4-D in order to quickly get new information and have a good basis for comparison with the company-produced data.

2. Continue its ongoing review of forest pest control practices. This review will evaluate all chemical and non-chemical controls to identify the most environmentally protective ways to control forest pests. The Agency believes that a piecemeal approach to forest chemical regulation only leads to confusion, both to the industry and to the public. Unless we review the whole range of possible controls, examining one chemical at a time only gives rise to questions about the chemicals which would be used to replace those examined and prohibited from use.

3. Review all new data as it comes in to determine if a change in our regulatory posture is warranted. This includes evaluating the results of new animal tests as well as looking into reported incidents involving human exposure to the chemical.

4. Continue to su port field tests to measure exposure to 2,4-D during the pr sent growing season.

5. EPA is informi g the Inter-Agency Work Group, established by the Whi e House to study the possible long-term effects of Agent Orang , of the actions being taken. EPA will also share its scienti ic findings with this committee.

IV. Toxicology Backgr und

The potential haza d of a chemical is usually measured in laboratory animal t sts. Animals are given doses of a chemical over a spec fic time period. Scientists attempt to derive from most of these tests a "no observable effect level" (NOEL) -- the d se level below the dosage where effects are first obse ved. From the animal tests and NOEL's, the potential ffects on humans and other animals can be estimated. A se of brief definitions is provided below to permit better understanding of the subsequent discussion of toxicolo ical findings.

A. General terms

1. Acute oral toxicity (LD50) - this test determines the dose l vel which produces death in half the test a imals after a single oral dose (short-ter test). Used to predict the near-term toxic ty of the chemical immediately upon contact wi h people or other non-target animals.

2. Chronic fe ding tests - animals are fed for most their life span (usually greater than 18 months in odents) in order to determine the dose level which shows no toxic effect in test animals. his is the test from which the NOEL is (usuall) derived.

3. Oncogenici y testing - animals fed relatively large dose of the test chemical for their life span (usua ly 18 months to 2 years in rodents) to try to nduce tumors. These tests are used to predict whether the chemical may pose a cancer haz rd.

4. Reproducti e testing - these tests evaluate the effects of the chemical on the fertility of both the male a id female parents by exposing the animals fo a period of time before breeding. The tests lso measure the possible effects of the chemic l on the pregnant female and the fetuses th ough several generations. (The test with odents through 3 generations runs approximat ly 14 months.)

5. Teratology testing - these tests evaluate the effects of the chemical on fetuses by exposing pregnant females during the short period of time that the fetus is most susceptible to congenital malformation. Teratogenic effects include cleft palate, central nervous system deformities, eye and limb deformities, and internal organ malfunction. These are considered to be life-threatening effects that put the animal at a disadvantage for surviving in its environment.

6. Fetotoxicity - fetotoxic effects can be seen in either the reproduction or teratology tests. Toxicity may be seen in the extreme form as fetal death or as less severe problems, such as delayed formation of bones, reduced body weights at birth, or edema (abnormal fluid accumulation in the tissue). Most fetotoxic effects appear to be reversible once exposure to the test chemical is curtailed. Therefore most fetotoxic effects are considered to be less serious than teratogenic effects, with the exception of fetal death.

B. Summary of Toxicology Review

Most of the data in EPA files on the potential health effects of 2,4-D are centered on the acid form, even though there are many derivatives, such as salts and esters. This is because the many forms of 2,4-D metabolize to the acid form in the environment and in the body. The discussion of animal data below, therefore, concerns the acid form of 2,4-D unless otherwise noted.

1. Acute toxicity - low to moderate. The potential for immediate poisonings from contact with the chemical is unlikely.

2. Neurotoxicity - There is little definitive information on the possible neurological effects of 2,4-D. In several reported cases of impaired nerve function, it was not known if the individuals were peculiarly sensitive to that type of effect or were exposed to other toxic materials.

3. Reproductive effects (effects on the unborn) - Tests have been conducted on rats, mice and hamsters to evaluate the possible reproductive effects of 2,4-D. 2,4-D causes some of the less serious fetotoxic effects, such as edema (swelling of tissues) at the lower dose levels tested, and causes life-threatening birth defects (skeletal malformations) and cleft palates only at the very high levels tested.

Based on available animal studies, EPA estimates that the level of exposure in a "worst case" situation (eg. a person standing directly under a spray plane) would be 500 to 1000 times less than the dose level that might cause an effect.

Much of the data available to judge these effects was generated by old study protocols, has deficiencies in the test methods, and needs clarification by further study.

EPA also reviewed summaries of tests conducted in Russia which state that some derivatives of 2,4-D produced adverse effects on unborn animal fetuses at much lower levels than indicated by the data in EPA's files. These summaries could not be used in the Agency's review because the identity of the test material, and its impurities, was unclear, and because there were no numerical data to back up the summary conclusions. In some cases tests need to be done on specific derivatives of 2,4-D.

4. Oncogenicity (potential for causing tumors) - Several rodent studies have been conducted to date. The tests were conducted a decade ago and are considered to be inadequte and inconclusive by today's scientific standards. New studies on rodents are needed.

5. Mutagenicity (inheritable effects) - The vast majority of the mutagenicity studies conducted on 2,4-D are negative. However, there are three positive studies. Taken as a group, the results of the studies can best be described as inconsistent and inconclusive. A new series of tests being conducted by the Department of Health, Education, and Welfare will be reviewed by EPA when they are completed.

6. Epidemiology - No epidemiological studies of human health effects from 2,4-D exposure have been completed. However, EPA is currenlty investigating reports about alleged adverse effects from potential chemical exposure in several parts of the country. EPA will be looking at the results of those studies and will decide in the near future about additional field work.

V. Exposure to 2,4-D

There are at least three ways that the average citizens might come into contact with 2,4-D - through the diet, during home use, and drift of the herbicide from nearby use.

a) Diet

The EPA has set tolerances for residues of 2,4-D in various food crops. The Food and Drug Administration (FDA) routinely samples a variety of foods (the Market Basket Survey) which FDA considers to be representative of the average American diet. Samples are analyzed for pesticide residues. During the period of 1974 to 1977, no 2,4-D residues were found in any of the products in the Market Basket Survey. However, during the 1965 to 1977 period, a variety of other food products were analyzed under other surveys in which about 1.1% were positive for 2,4-D in very minute quantities that were well below EPA's tolerance (allowable residue) levels.

b) Home use

There are currently a number of registered home-use products which contain 2,4-D in a variety of formulations. Exposure to the herbicide in home-use situations will depend to some extent on the specific formulation used. If care is exercised by the homeowner in adhering to the directions for use and precautionary statement on the label, exposure to 2,4-D should be low.

c) Drift

"Drift", the airborne transport of pesticide materials to a non-target area, is a common source of exposure. Sometimes, a pesticide will drift during application, depending on climatic conditions (temperature, wind speed), type of formulation used, terrain (forests, mountains), and type of application method used (aerial, ground spray). Several States have imposed restrictions on 2,4-D use in order to cut down on drift potential.

Once on the ground or target crop, the herbicide may become airborne again by the process of vaporization. This particular type of drift has been the subject of intensive research by the producers of 2,4-D. Since the introduction of less volatile forms of the herbicide over the last few years, this kind of drift has become much less extensive.

VI. Environmental Persistence

2,4-D is not a persistent pesticide. Breakdown of the herbicide begins almost immediately after application at a rate dependent on several environmental factors such as temperature, humidity and medium (air, soil, crop, water). The rate of loss (commonly referred to as the half-life) is a measure of the time required for half of the substance to be degraded or lost.

On sprayed vegetables, the half-life varies from 1-3 weeks depending on geographic location, climatic conditions, vegetation type, application technique and formulation used.

In soil, the half-life varies from several days to 2 weeks, depending on acidity, soil type and amount of rain.

In water, the half-life varies from a few days to several months depending on factors such as oxygen concentration, acidity, light intesity, water temperature and formulation used.

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